



PATENT

UNITED STATES PATENT AND TRADEMARK OFFICE  
(Case No. MBHB00-919-D 250/111)

In re Application of:

Thompson

Serial No.: 09/630,846

Filing Date: August 2, 2000

For: IMPROVED POLYMEARASE III  
BASED EXPRESSION OF  
THERAPEUTIC RNAs

Group Art Unit: 1635

Examiner: Lacourciere, K.

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Commissioner for Patents  
Washington, D.C. 20231

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Dear Sir:

Pursuant to 37 C.F.R. Section 1.97 - 1.99, the Applicant wishes to make the following references listed on the enclosed Form PTO-1449 of record in the above-identified application. Copies are also listed in the PTO-1449 form enclosed herewith. It is requested that the documents be given careful consideration and that they be cited of record in the prosecution history of the present application so that they will appear on the face of the patent issuing from the present application.

**CITED REFERENCES**

**Other Documents (Including Author, Title, Date, Pertinent Pages, Etc).**

1. Cameron and Jennings, "Specific Gene Expression by Engineered Ribozymes in Monkey Cells," Proc. Natl. Acad. Sci. USA 86:9139-9143 (1989).

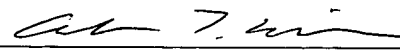
**CERTIFICATE OF MAILING (37 C.F.R. 1.8a)**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the: Commissioner for Patents, Washington D.C. 20231, on February 7, 2002.

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Andrew W. Williams

2. Cushman et al., 1996, "Ribozyme Inhibition of VEGF-Mediated Endothelial Cell Proliferation in Cell Culture and VEGF-Induced Angiogenesis in a Rat Corneal Model" Abstract in IBC USA Conferences-Angiogenesis Inhibitors.
3. Desjardins et al., "Pharmacokinetics of a Synthetic, Chemically Modified Hammerhead Ribozyme Against the Rat Cytochrome P-450 3A2 Mrna After Single Intravenous Injections," J. Pharmacology and Experimental Therapeutics 27(8):1419-1427 (1996).
4. Efrat et al., "Ribozyme-mediated attenuation of pancreatic  $\beta$ -cell glucokinase expression in transgenic mice results in impaired glucose-induced insulin secretion," Proc. Natl. Acad. Sci. USA 91:2051-2055 (1994).
5. Flory et al., "Nuclease-resistant ribozymes decrease stromelysin mRNA levels in rabbit synovium following exogenous delivery to the knee joint," Proc. Natl. Acad. Sci. USA 93:754-758 (1996).
6. Larsson et al., "Reduced  $\beta$ 2-microglobulin mRNA levels in transgenic mice expressing a designed hammerhead ribozyme," Nucleic Acids Research 22(12):2242-2248 (1994).
7. Lieber and Kay, "Adenovirus-Mediated Expression of Ribozymes in Mice," Journal of Virology 70(5):3153-3158 (1996).
8. Lyngstadaas et al., "A synthetic, chemically modified ribozyme eliminates amelogenin, the major translation product in developing mouse enamel in vivo," EMBO J. 14:5224-5229 (1995).
9. Malone et al., "Cationic liposome-mediated RNA transfection", Proc. Nat. Acad. Sci. USA 86:6077(1989).
10. RPI Press Release, Aug. 29, 2001, [http://www.prnewswire.com/cgi-bin/micro\\_stories.pl?ACCT=742975&TICK=RZYM&STORY=/www/story/08-29-2001/0001562763&EDATE=Aug+29,+2001](http://www.prnewswire.com/cgi-bin/micro_stories.pl?ACCT=742975&TICK=RZYM&STORY=/www/story/08-29-2001/0001562763&EDATE=Aug+29,+2001).
11. RPI Press Release, June 20, 2001, [http://www.prnewswire.com/cgi-bin/micro\\_stories.pl?ACCT=742975&TICK=RZYM&STORY=/www/story/06-20-2001/0001517763&EDATE=Jun+20,+2001](http://www.prnewswire.com/cgi-bin/micro_stories.pl?ACCT=742975&TICK=RZYM&STORY=/www/story/06-20-2001/0001517763&EDATE=Jun+20,+2001).
12. RPI Press Release, Oct. 8, 2001, [http://www.prnewswire.com/cgi-bin/micro\\_stories.pl?ACCT=742975&TICK=RZYM&STORY=/www/story/10-08-2001/0001586793&EDATE=Oct+8,+2001](http://www.prnewswire.com/cgi-bin/micro_stories.pl?ACCT=742975&TICK=RZYM&STORY=/www/story/10-08-2001/0001586793&EDATE=Oct+8,+2001).

13. Sambrook et al. (Molecular Cloning, A Laboratory Manual, 2nd ed., 1989, sections 16.30-.32).
14. Seachrist, Bioworld Today, January 15, 1997, at <http://www.bioworld.com/bw/static.htm?path=br/data/bt01151997/bt01151997e.html>.
15. Sioud, "Ribozyme modulation of lipopolysaccharide-induced tumor necrosis factor- $\alpha$  production by peritoneal cells in vitro and in vivo," Eur. J. Immunol. 26:1026-1031 (1996).
16. Uhlmann and Peyman, "Antisense Oligonucleotides: A New Therapeutic Principle," Chemical Reviews 90:544-584 (1990).
17. Yamamoto et al., "Abrogation of Lung Metastasis of Human Fibrosarcoma Cells by Ribozyme-Mediated Suppression of Integrin  $\alpha 6$  Subunit Expression," Int. J. Cancer 65:519-524 (1996).

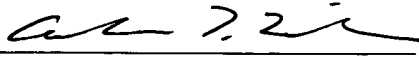
It is requested that each document cited be given thorough consideration and that it be cited of record in the prosecution history of the present application by initialing on Form PTO-1449. Such initialing is requested even if the Examiner does not consider a cited document to be sufficiently pertinent to use in a rejection or otherwise does not consider it to be prior art for any reason. This is requested so that each document becomes listed on the face of the patent issuing on the present application.

Portions of the references may be material to the examination of the pending claims, however no such admission is intended. 37 C.F.R. 1.97 (h). The references have not been reviewed in sufficient detail to make any other representation and, in particular, no representation is intended as to the relative importance of any portion of the references. This Statement is not a representation that the cited references have effective dates early enough to be "prior art" within the meaning of 35 U.S.C. sections 102 or 103.

This Information Disclosure Statement is in compliance with the continuing duty of candor as set forth in 37 C.F.R. Section 1.56. This Information Disclosure Statement is being filed before the mailing date of a final action, pursuant to 37 C.F.R. Section 1.97(c) and the fee set forth in Section 1.17(p), \$180.00, is enclosed.

Respectfully submitted,

Date: February 7, 2002

  
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Andrew W. Williams  
Registration No. 48,644